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MARY SHELLEY, FRANKENSTEIN, AND THE DARK SIDE OF MEDICAL SCIENCE

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In 2010, I was asked to give a presentation on Mary Shelley (Figure 1) and her views on medical science in conjunction with a visit by the National Library of Medicine's Frankenstein exhibit to our campus. Before that time, I knew virtually nothing of Mary Shelley, and what I knew of her Gothic novel, I owed entirely to Boris Karloff's film portrayal of Frankenstein's monster. What I'm about to share with you is what I subsequently learned about Shelley, her famous novel, and the lessons it contains regarding the dark side of medical science.

In 1818, when Shelley was just 18, she, her poet husband, and John Polidori (creator of the vampire genre of fantastic fiction) were guests of Lord Byron at his villa on Lake Geneva at one of the most famous house parties in literary history. The four spent a great deal of time discussing the increasingly blurred boundary between life and death. They wondered if the origin of life could be discovered, if scientists could galvanize or electrically reanimate a corpse. . . if it were possible to create a humanoid (1).

One evening, Byron proposed a competition to see who among them could create the best ghost story. Mary's entry was *Frankenstein* (2), a story that she claimed had come to her as a nightmare, and one that she believed would terrify others as much as it had her (1).

Mary Shelley's *Frankenstein* resembles the Boris Karloff version of the story only slightly. It is narrated by Robert Walton, a scientist, who, like the protagonist, Victor Frankenstein, is totally consumed by his research. The story concerns an 8-foot monster pieced together by Frankenstein from body parts collected in charnel houses. Exactly how it is brought to life is never revealed. However, Shelley later intimated that galvanism (electrical stimulation) was the life-giving procedure (3).

The monster has no name, is hideous to behold, and is not merely

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FIG. 1. Richard Rothwell's 1840 portrait of Mary Shelley.

vocal but eloquent. It begins life as a sensitive, caring being, but because of its hideous appearance, it is forever shunned. The more it is excluded, the more it envies, the more it destroys, the more it is excluded (4). It is mortal, and at the end of the book, after having destroyed its creator, the monster disappears into the arctic ice field "to sleep in peace."

Shelley's book is a social commentary, highly critical of society as well as the church. However, its principal theme concerns the prototypic scientist, his character, his motives, his sense of gratification, and also the unanticipated consequences of his work. Most of all, it is a cautionary tale that even today speaks to the promise and the perils of scientific advances.

Frankenstein was the first of a new genre of horror stories, and on cursory examination, one is inclined to dismiss it as nothing more than an absurd and outdated anti-science manifesto. The story strikes one as preposterous, and yet it is also strangely unsettling. As one delves deeper into its meaning, one wonders: Can the dead actually be brought back to life? Could medical science's potential for harm be as great as Shelley implies? What motivates medical scientists to do what they do, and does it matter? Should scientists be held as responsible for the harm their discoveries cause as for the benefits?

In her novel, Shelley has her protagonist create a living monster out of parts collected from various corpses. In doing so, Frankenstein is motivated not by a desire to serve mankind, but "to become one among those whose names are recorded in glory." Banishing "disease from the human frame" was a goal only in so far as it brought him fame. And fame did come to him when he succeeded in raising the dead. . . Preposterous?. . . Is it possible to bring the dead back to life? Well, that depends on how one defines "dead."

Some would say that cardiopulmonary resuscitation (CPR) is a process by which "dead" people are brought back to life, and in which galvanism plays no small role. Early in the 18th century, frictional machines were used to produce sparks and electrostatic electricity, much to the entertainment of the leisured classes. In the 1790s, Luigi Galvani (1737–1798), for whom galvanism is named, showed that electricity generated by the recently invented Leyden jar (Figure 2) could make the muscles of dead frogs twitch. Based on these experiments, he pioneered the concept that electricity is the "vital juice" that runs from its source in the brain through nerves to activate muscles (far-fetched?. . . not really!). Later, foreshadowing the reanimation evoked in *Frankenstein*, he progressed from studies involving artificial electricity to ones involving atmospheric electricity (ie, lightning). His nephew, Giovanni Aldini (1762–1834), subsequently showed that facial grimaces and jaw movements could be evoked in recently executed criminals by passing an electrical current through their exposed brains (Figure 3). Mary Shelley was apparently aware of these experiments when she wrote *Frankenstein* (5, 6).

The first successful use of electricity in CPR most likely occurred in 1774, when a 3-year-old girl who had fallen from a first-story window was revived by electrical shocks applied to her chest that were generated by a Leyden jar (7). Two centuries would elapse before this remarkable achievement would become routine clinical practice.

Today, sudden cardiac death accounts for approximately 500,000 deaths annually in North America (8). When current CPR techniques

FIG. 2. Drawing of an early Leyden jar.

are performed on patients arresting outside of the hospital, more than a quarter survive long enough to be admitted to a hospital (9–12). Given these statistics, approximately 125,000 lives could be saved each year if defibrillators were widely available and the general public properly trained in CPR techniques. In the hospital, where in developed countries 1 to 5 patients of 1000 has a cardiac arrest, CPR brings fewer victims back to life (only 14% to 22% by some estimates), but because hospitalized patients are generally sicker than their outpatient counterparts, one would expect them to have poorer outcomes (13–16).

However, CPR, whether performed in the hospital or out in the community, takes time to organize. What if it were possible to initiate CPR immediately, at the very moment an otherwise fatal cardiac arrhythmia arose? Think of the lives that could be saved.

Of course, Michel Mirowski (Figure 4) made this possible by inventing his implantable cardioverter-defibrillator (ICD). Similar to Frankenstein, he seems not to have been motivated primarily by a desire to relieve the burden of human disease in developing his device. When interviewed by John Kastor, a former chairman of medicine at the

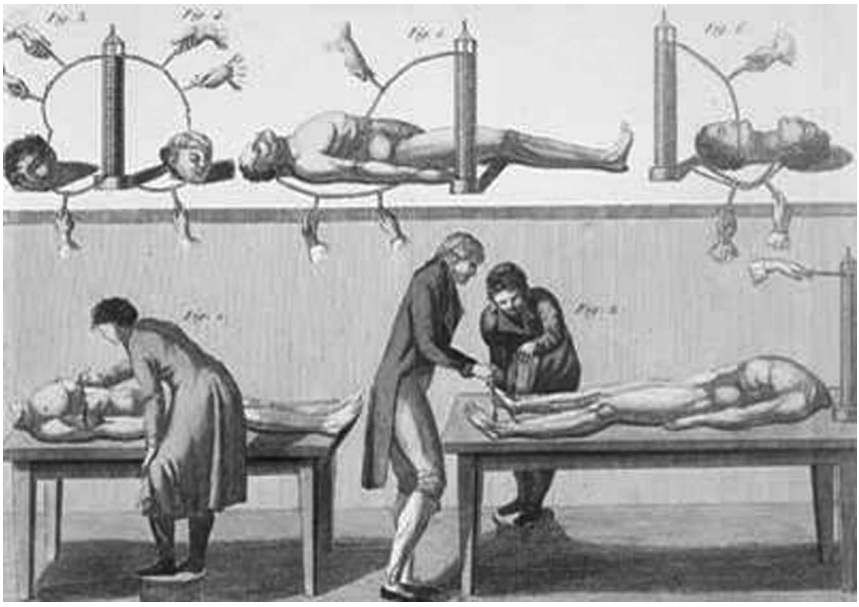

FIG. 3. Early illustration of Giovanni Aldini's electrical experiments on recently executed criminals.

University of Maryland, Mirowski said simply that he was driven by "an internal need to investigate and create" (17).

On February 4, 1980, the first ICD was implanted in a 57-year-old woman with drug-resistant, recurrent ventricular tachycardia and fibrillation at the Johns Hopkins Hospital (17). Today, approximately 100,000 US patients have ICDs installed each year (18). No one knows for certain how many lives are actually saved by ICDs. However, in theory, the number is enormous. If so, what possible relevance could Mary Shelley's dark view of raising the dead have for us today?

Few today would dispute the view that medical science has been responsible for extraordinary advances in human health and social well-being. Patients with what were once terminal illnesses, such as tuberculosis, congenital heart defects, and immunodeficiency disorders, now grow old. Transplanted organs give normal lives back to patients with dead kidneys, livers, and hearts. Those who are crippled have knees and hips replaced and can play tennis again.

And yet, all is not bright in our profession. Medicine has its dark side with a potential for harm that some believe is as pervasive as it is widely ignored. A spectacular example of this potential concerns the recent creation of a highly contagious strain of the H5N1 bird influenza virus by Dutch scientists that has raised fears of a laboratory-induced

FIG. 4. Michel Mirowski, inventor of the implantable cardioverter-defibrillator.

pandemic or biological attack capable of killing hundreds of millions of people (19). The cloning of "Dolly" by Scottish researchers in 1997 (20) has raised additional fears of science and technology, not to mention questions about what constitutes "acceptable science." In synthesizing an entire bacterial genome to create the planet's first artificial self-replicating species, Craig Venter, similar to his counterpart in Shelley's novella, became a self-proclaimed "modern Prometheus*" (21). Venter's contention that artificially manufactured microbes could be of great benefit to mankind by producing vaccines, bio-fuels, and such has done little to dispel fears of Friends of the

*In some versions of Greek mythology, Prometheus, the giver of fire, was also the Titan who created man.

Earth, an environmental group concerned that such life forms would have a devastating effect on the global ecology if they were to escape from the laboratory.

These, however, are theoretical examples of medical science's dark side. Adverse drug reactions (ADRs) are real examples. Nearly 500 years ago, Paracelsus (Figure 5), one of three scientists Shelley invokes in *Frankenstein*, pioneered the use of chemicals in medicine. Diseases, he claimed, were caused by poisons which could be expelled by poisons if administered in proper doses (22). His chemicals, similar to those we use today to treat patients, were, in effect, poisons with beneficial side effects . . . a concept long since forgotten.

In the aggregate, such chemicals (i.e., drugs) almost certainly cause more harm to our patients than almost anything we do to them. An

FIG. 5. Copy of a lost 17th century portrait of Paracelsus by Quentin Massys.

estimated 3% to 6.5% of hospital admissions in the United States are precipitated by an ADR, of which 1% is fatal. During the first few weeks after discharge, another 11% to 17% of patients experience an ADR (23, 24). Given these statistics and the 37 million hospital admissions in the United States each year (25), the cost of ADRs in terms of mortality, not to mention morbidity, is enormous. Similar to Frankenstein's monster, which began life as a benign being, new drugs invariably appear more effective and less toxic (though more expensive) than old drugs. Only later, in the post-marketing period, is the full extent of their dark side revealed.

What of CPR? What could possibly be the dark side of a medical intervention that snatches from the very jaws of death a substantial number of patients victimized by sudden cardiac arrest? Although nearly a quarter of patients receiving CPR outside of the hospital survive long enough to be admitted to a hospital, less than 10% survive to hospital discharge, and of those who do, one in four is left with severe neurological deficits (9–12). How long such patients live on average after leaving the hospital is not addressed in any of the many publications dealing with CPR, at least not the ones I could find. Patients undergoing CPR in the hospital fare only slightly better with just 10% exhibiting severe neurological deficits at the time of discharge, although nearly a third leave with "significant neurological disability" (13–16).

There is little doubt that Mirowski's ICD prevents sudden cardiac death, but at what cost? In terms of dollars, the device costs something in the range of $3 billion annually (100,000 devices at approximately $30,000 each) (26). The return on this large financial investment is not known for certain. However, it has been estimated that patients receiving an ICD to prevent recurrence of a malignant arrhythmia (secondary prevention) live, on average, only 8 months longer than those treated with maximal medical therapy alone. Patients receiving an ICD for primary prevention (those at risk of a fatal arrhythmia but not yet having experienced one) live an average of 6 months longer than their medically treated counterparts (27). The cost in terms of decreased quality of life for this modest increase in survival time is substantial. Seven percent of men and 14% of women experience major complications related to their ICDs, such as lead displacement, electrical storm, infection, pneumothorax, and such. Moreover, nearly a quarter of the ICD shocks are inappropriate (ie, prompted by something other than ventricular tachycardia or fibrillation), which creates an ongoing sense of dread that some patients find intolerable and ask for their devices to be turned off (27). On a bit brighter side, improved

programming of these devices has recently shown promise of reducing the number of inappropriate shocks delivered (28).

What of knowledge in general, the pursuit of which is at the heart of Shelley's book? As Victor Frankenstein's life draws to its tragic end, he warns Walton: "learn from me; if not by my precepts, at least by my example, how dangerous is the acquirement of knowledge." Does his warning have relevance for us as physicians today? Does medical knowledge itself have a dark side? Is it possible that we have been misguided in exhorting our trainees that they can never know enough about their patients?

In fact, mounting evidence generated largely in response to fiscal pressures, confirms the concept that sometimes, perhaps more times than we realize, it is best not to know everything there is to know about a patient. Consider, for example, the routine annual physical or the screening of asymptomatic elderly men for prostate cancer. It is becoming increasingly evident that abnormalities identified on such routine examinations are just as likely to lead to harm as to benefit. Consider the case of one of our recently departed members, who decided to take advantage of an offer to have a free whole body CT scan when the study was first being introduced at his hospital. Although in excellent health at the time, his "free" CT scan revealed calcium deposits in his coronary arteries. This led to a series of additional tests, culminating in a coronary angiogram that showed non-critical coronary artery narrowing consistent with his age. A cholesterol plaque dislodged during the angiogram found its way to his eye, causing double vision, which, fortunately was temporary. Nearly two decades later, our fellow ACCA member died of chronic lymphocytic leukemia, never having developed symptoms of coronary artery disease.

This phenomenon, one in which a serendipitous finding compels a physician to order additional unnecessary and potentially dangerous tests, has been called the "tar baby syndrome" after the Uncle Remus fable of the same name (29) (Figure 6). In the case I have just described, the tar baby was the whole body CT scan, which once "touched" would not let go until our former member had found his way to the cath lab for the final examination in a series of procedures that should never have been performed.

Why are we so inclined to ignore medical science's dark side? Partly, it is because as physicians we have serious conflicts of interest that compel us to do so. However, our patients have no such conflicts, and yet, in many ways, they are even more obsessed with medicine's bright side than we are. How can this be? There are several possible explanations.

First, medical science has produced so many miracles in recent years

FIG. 6. Scene from Walt Disney's "Tar-Baby" cartoon.

our ability to relieve suffering and extend life seems limitless. However, in all too many instances, rhetorical strategies are used to exaggerate these miracles. Findings are called evidence (a term connoting proof), rather than data (a neutral term), when proof is only rarely the outcome of clinical investigations. Ratios, rather than absolute values, are used to report outcomes to give the appearance of greater treatment effects than are actually achieved. Complications are underreported. Too often treatment benefits are highlighted even in trials with statistically insignificant results; and when statistical significance is achieved, too often it trumps clinical significance. Interventions are said to save lives, when, at best, they simply extend lives long enough for patients to die of some disorder other than the one being studied. Clinical investigators rarely report the number of extra years their interventions add to patients' lives. Nor do they consider the possibility that the decrease in mortality from the disease being treated simply reflects an increase in mortality due to some other disorder for which the treatment might be responsible (30).

All this is not to say that we do not owe medical scientists an enormous debt of gratitude for having helped extend our lives and relieve our suffering. They richly deserve to be venerated. Should they also be held accountable for the unintended harm their discoveries cause? Shelley seemed to think so. "You," Frankenstein's monster says to him, "do not reflect that you are the cause of [my] excess!"

Alfred Nobel (Figure 7) apparently was motivated by the sting of such criticism when he created his eponymous prizes, one of which

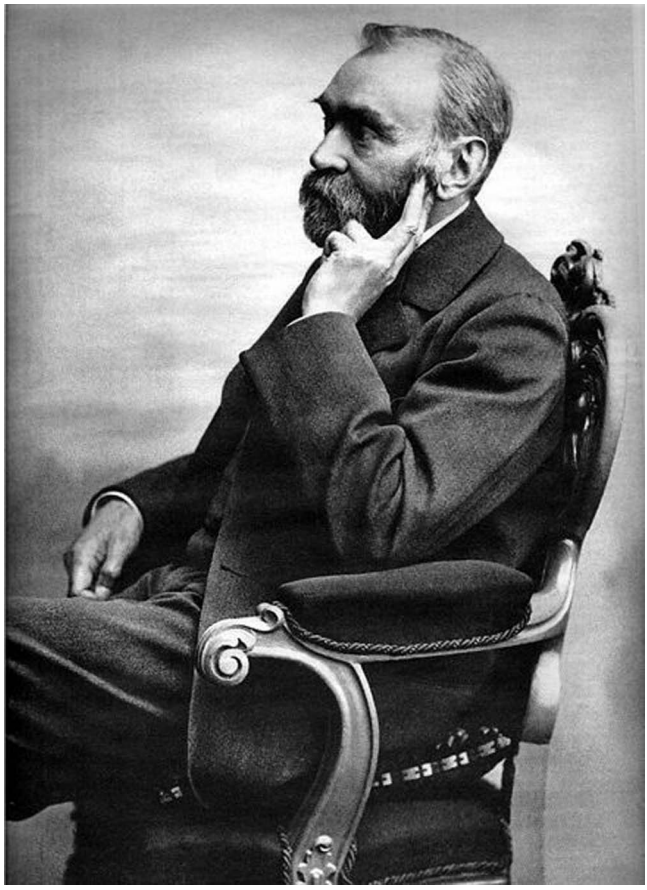

FIG. 7. Photograph of Alfred Nobel taken by Gösta Florman (date unknown).

honors medical scientists. According to the standard story of his decision to endow the prizes, when his brother died in 1888 while visiting Cannes, a French newspaper mistakenly identified Alfred as the one who had died, and in the obituary condemned him as a "merchant of death" for having invented dynamite. Ignoring the many good things his discovery had made possible for miners, engineers, and builders, the paper excoriated Nobel for having become rich by finding a way to kill people faster than ever (31).

Michel Mirowski has never been subjected to such attacks and probably never concerned himself with the dark side of his invention. Although the ICD has a clear potential to extend life, albeit only modestly and at considerable expense, it has its down side. Extending life is but one goal of medical science and not necessarily its most

important one. It also strives to relieve suffering and increase the quality of life, which the ICD does not; to facilitate activities of daily living, which the ICD does not; and as much as possible, to rob death of its terrors by helping patients die with a minimum of suffering, which the ICD does not. For at least some patients, the ICD's principal effect is merely to prolong old age and feebleness.

Mary Shelley's mother died of a peri-partum infection in 1797, shortly after the birth of her famous daughter, and 21 years before the birth of Ignaz Semmelweis, who later showed the world how to prevent these tragic infections. When Mary was 17, she eloped with Percy Bysshe Shelley. Two years later they were married. In another two years he drowned off the coast of Livorno, Italy. At the time of his death, Percy was considered a minor poet, whereas Mary was already a renowned novelist. Mary Shelley died in 1851 at the age of 54 after an 11-year illness of nervous irritability, headaches, and depression, thought to have been caused by an enlarging meningioma. Dr Richard Bright of Guy's Hospital treated her with opium (3). More could be done for her today, although possibly less than we might hope.

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